

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT**NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)**

(PCT Rule 44bis.1(c))

To:

ELEND, Almut, Susanne
Venner, Shipley LLP
20 Little Britain
London EC1A 7DH
ROYAUME-UNI

RECEIVED

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Date of mailing (day/month/year)

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Applicant's or agent's file reference

45772PCT1

IMPORTANT NOTICE

International application No.

PCT/GB2004/002579

International filing date (day/month/year)

15 June 2004 (15.06.2004)

Priority date (day/month/year)

18 June 2003 (18.06.2003)

Applicant

GENERICIS (UK) LIMITED et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Nora Lindner

Facsimile No.+41 22 740 14 35

Facsimile No.+41 22 338 89 65

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 45772PCT1	FOR FURTHER ACTION	See item 4 below
International application No. PCT/GB2004/002579	International filing date (<i>day/month/year</i>) 15 June 2004 (15.06.2004)	Priority date (<i>day/month/year</i>) 18 June 2003 (18.06.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant GENERICIS (UK) LIMITED		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

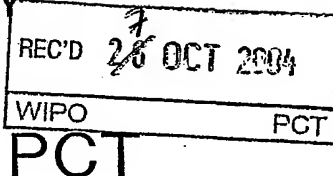
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|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 19 December 2005 (19.12.2005)
Facsimile No. +41 22 740 14 35	Authorized officer <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Nora Lindner</div> Telephone No. +41 22 338 89 65

INTERNATIONAL PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY



To:

see form PCT/ISA/220

29/12

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/002579

International filing date (day/month/year)
15.06.2004

Priority date (day/month/year)
18.06.2003

International Patent Classification (IPC) or both national classification and IPC
C07D495/04, A61K31/5513, A61K9/00

Applicant
GENERICS [UK] LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Steendijk, M

Telephone No. +49 89 2399-8460



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/002579

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/002579

Box No. II Priority

1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/002579

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 28-34

because:

- ☒ the said international application, or the said claims Nos. 28-34 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/002579

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-34
	No: Claims	
Inventive step (IS)	Yes: Claims	1-34
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-27
	No: Claims	

2. Citations and explanations

see separate sheet

1) The present application relates to an amorphous form of olanzapine, methods for its preparation and its application in pharmaceutical formulations.

2) Cited documents:

D1: US-A-5 457 101 (GREENWOOD BEVERLEY ET AL) 10 October 1995 (1995-10-10)

D2: WO 03/007912 A (DEKEMPER KURT DOUGLAS ; NAIL STEVEN L (US); FITES ALAN LEE (US); LILLY) 30 January 2003 (2003-01-30)

D3: WO 02/094236 A (ALEXZA MOLECULAR DELIVERY CORP) 28 November 2002 (2002-11-28)

D4: CHUE PIERRE ET AL: "Dissolution profile, tolerability, and acceptability of the orally disintegrating olanzapine tablet in patients with schizophrenia." CANADIAN JOURNAL OF PSYCHIATRY. REVUE CANADIENNE DE PSYCHIATRIE. OCT 2002, vol. 47, no. 8, October 2002 (2002-10), pages 771-774, XP002300476 ISSN: 0706-7437

D5: DRUGS AND THERAPY BULLETIN, vol. 17, no. 4, April 2003 (2003-04), pages 1-4, XP002300477

3) Novelty

Document D1 already describes a freeze dried formulation of olanzapine for injection (see example 3), in which olanzapine may be presumed to be in amorphous form.

Document D2 describes similarly a freeze dried form of olanzapine, in particular for preparing injection-formulations, and explicitly mentions the amorphous form of the product (see claim 3).

Document D3 describes formulations for preparing aerosols of olanzapine, in which the agent is to present predominantly in the amorphous form (see page 20, see also example 3).

Documents D4 and D5 describe orally disintegrating tablets of lyophilized olanzapine, in which the olanzapine may be presumed to be in amorphous form.

In this context it is further observed that the method of claims 6-7 is not specifically described in documents D1-D5. It should however be noted that any melting point determination on known crystalline olanzapine will involve melting as defined in claim 6 with eventual subsequent cooling in line with claim 7

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2004/002579

4) Inventive step

In as far as any subject-matter could be identified in the present application, no basis for an inventive step can at present be recognized.

In this context, it is noted that the relatively high Tg and stability of the amorphous form reported in the present application (see page 10) may not have been explicitly mentioned in the available prior art, but should not have surprised the person skilled in the art in view of the availability of commercial products such as mentioned in for instance D5.

5) Further observations

Claims 28-34 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).